

### **REMARKS**

Reconsideration of the above-identified application in view of the amendments above and the remarks following is respectfully requested.

Claims 1-5, 8 and 11-22 are in this case. Claims 11-19 and 22 were withdrawn under a restriction requirement as drawn to a non-elected invention. Claims 1-5, 8, 20 and 21 have been rejected. Claims 1 and 22 have now been amended.

### ***Election/Restriction***

The Examiner states that newly submitted claim 22 is not directed to an invention originally claimed to form a single general inventive concept under PCT rule 13.1 and that restriction to one of inventions I-IV is required. Due to a typographical error stemming from an auto correct function of Microsoft Word, claim 22 language was erroneously auto-corrected and the term "calcein" was erroneously replaced with "calcitonin". Claim 22 has now been amended to correct this typographical error and re-associate claim 22 with the presently elected group I invention.

### ***35 U.S.C. § 112, First Paragraph, Rejections***

The Examiner has rejected claims 1-5, 8 and 20-21 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Examiners rejections are respectfully traversed. Claim 1 has now been amended.

The Examiner points out that the amendment filed November 5, 2005 appears to introduce new matter into the disclosure. The added material that is not supported by the disclosure is the phrase "marker dissociated from said metal ion" of claim 1.

This phrase has now been amended to recite "marker released from said metal ion". Release of the marker from the iron via iron chelation is described throughout the application, see for example step (d) described in the beginning of the summary section.

Accordingly, section (b) of claim 1 now recites "said iron chelator of said polymer-conjugated form of said iron chelator chelates said metal ion of said complex to thereby release said marker from said metal ion".

In view of the above arguments and claim amendments, Applicant believes to have overcome the 35 U.S.C. §112, first paragraph, rejections.

### ***35 U.S.C. §112, Second Paragraph, Rejections***

The Examiner has rejected claims 1-5, 8 and 20-21 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The Examiner's rejections are respectfully traversed. Claim 1 has now been amended.

The Examiner states that in claim 1 step (a), the phrases "with a surface coated" and "with a polymer conjugated iron chelator" are indefinite since the identity of the object of these phrases is not clear.

Applicant firmly believes that claim 1 is definite in its language and that an ordinary skilled artisan would be well aware of the objects described by the above referenced phrases. However, in the interest of expediting prosecution of this case, claim 1 has now been amended to recite: "contacting the sample of biological fluid with a surface coated with a polymer-conjugated form of an iron chelator". A "polymer-conjugated form of a metal chelator" is described and exemplified by the specification and thus Applicant believes that such a phrase would be clear to the ordinary skilled artisan. Such an amendment also makes it abundantly clear that the object in question does not contain iron, but is rather an iron chelator which is conjugated to a polymer.

The Examiner states that the term "allowing" and the phrase "to be chelated" recited in claim 1 step (a) are indefinite.

The Examiner also states that the overall purpose of "allowing the non-bound iron in the sample of biological fluid to be chelated by said polymer conjugated iron chelator" is indefinite in view of step (b), wherein said polymer-conjugated metal chelator chelates said metal ion.

The Examiner further states that step (b) is also indefinite in its recitation of phrases describing the complex, marker and metal ion and the role of the iron chelator.

Claim 1 has now been amended to clearly identify the role of the iron chelator (conjugated to the polymer) as that which:

- a) ... "chelates the non-bound iron in the sample of biological fluid";
- and
- b) ... "chelates said metal ion of said complex to thereby release said marker from said metal ion;"

Thus, the iron chelator (conjugated to the polymer and coated on the surface) serves two roles, it chelates any unbound iron present in the biological sample (step a) and it also chelates iron ions of a marker complex (step b).

While step (a) ensures that the non-bound iron present in the sample is captured by the chelator, step (b) quantifies the unbound sites of this chelator, i.e., the chelator sites which are left unbound following step (a). Quantification of unbound sites is effected by using a complex which includes a marker bound to a metal ion (which can be iron or another metal which can be chelated by the iron chelator). By exposing the polymer-conjugated chelator (coated on a surface) to this complex, any unbound chelator sites will chelate the metal ion of the complex thereby releasing marker molecules from the complex which can be quantified. The quantity of such "free" marker molecules directly correlates with the number of unbound surface-conjugated chelator sites and thus provides a measure of the number of iron-bound chelator sites and of the quantity and concentration of NTBI in the sample.

### ***35 U.S.C. §103(a) Rejections***

The Examiner has rejected claims 1-2, 5 and 20-21 under 35 U.S.C. §103(a) as being unpatentable over Tobacco et al. (US 4,703,015) in view of Charlton (US 4,734,375).

The Examiner states that Tobacco et al. describe a method for determining the concentration of iron in a sample. The Examiner further states that Tobacco et al.

contact the sample with a polymer-conjugated iron chelator (Column 2 lines 65-66) and a marker bound to an iron chelator (column 3 lines 59-60).

As is clearly described hereinabove with respect to the 112 rejection the iron-marker complex utilized by the present invention serves to quantify any unbound sites present on the iron chelator following a step of exposing the chelator to a biological sample containing non-bound iron.

Contrary to the Examiner's assertion, the iron bound marker complex utilized by Tobacco et al. is not utilized for quantifying unbound chelator sites on a polymer-conjugated chelator, but rather serves to quench any impurities in the sample which might affect the calorimetric value obtained from the polymer-conjugated chelator reaction.

Tobacco et al. utilize two reagents (column 3 lines 3-10):

- (i) a chromogenic reagent which serves to directly determine the concentration of free iron in the sample, this chromogenic reagent modifies the optical properties of a solution (as measured via optical density) according to the amount of iron it binds; and
- (ii) a masking reagent which serves to bind any components present in the sample which may affect the functionality of the chromogenic agent.

The function of each of these components in quantifying iron in a sample is described in column 3, lines 37-68.

As is clearly stated therein, the chromogenic agent can be used without the masking agent to directly quantify iron concentration of a sample. This is effected by adding the chromogenic agent to the sample and reading the optical density of the sample against a control "blank chromogenic agent" (a chromogenic agent which is not exposed to the sample).

In cases where the sample is suspected to contain substances which can interfere with the ability of the chromogenic agent to bind iron or to accurately reflect the concentration of iron present the sample, Tobacco et al. utilize an additional masking step which prevents any interfering substances (e.g. beta-lipoprotein) present in the sample from affecting iron quantification by preventing association of such substances with the chromogenic agent.

The calorimetric reagent mentioned by Tobacco et al. is in fact a composition (or kit) which includes two solutions, the chromogenic reagent solution for directly measuring iron concentration; and the masking reagent solution which functions in preventing association between the chromogenic agent and any interfering substances (see column 2, lines 19-28).

From the forgoing it is clear that Tobacco et al. do not utilize a marker complex for indirectly measuring iron concentrations as is effected by the present invention, rather, Tobacco et al. utilize a chromogenic agent for directly measuring iron concentration and a masking agent for quenching any interfering substances present in the sample.

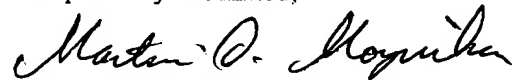
Since Tobacco, et al. describe an iron quantification approach which differs both in concept and operation from the iron quantification method of the present invention, it is Applicants' strong opinion that the combination of Tobacco et al. and Charlton which teaches surface coated complexes would not motivate the ordinary skilled artisan to make the present invention.

It is also Applicants' strong opinion that the combination of Tobacco et al., Charlton and additional references which teach the use of desferrioxamine (Yegorov et al.; cited with respect to the 103 rejection of claims 3), multiwell plates (Guire and Chudzik; cited with respect to the 103 rejection of claims 4) or calcein (Breuer et al.; cited with respect to the 103 rejection of claims 8) would not render obvious the present invention as claimed.

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In view of the above amendments and remarks it is respectfully submitted that claims 1-5, 8 and 20-22 are now in condition for allowance. Prompt notice of allowance is respectfully and earnestly solicited.

Respectfully submitted,



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Encl.

Petition for Extension of Time (2 months)